REMARKS

Claims 21-33 were pending. Claims 24-25 and 29-33 are canceled herein. New claims 34 and 35 are added herein. Claims 21, 23, 26 and 28 are amended herein. Support for the new and amended claims are found throughout the specification at, *e.g.*, Example 8. Therefore, it is believed that no new matter is added. The amendments and cancellations are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and cancelled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future applications. Claims 21-23, 26-28, and 34-35 are currently pending. No claim is allowed.

Formal Matters

Applicants gratefully acknowledge the entry of the amendment and response filed April 21, 2003 (Paper No. 9) and the withdrawal of the previously pending rejections.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 21-33 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. According to the Action, the term "gpIIbIIIa" is indefinite in 21, 26, and 31-32 because the acronym or abbreviation must be fully defined and recited in at least one claim. Applicants traverse this rejection.

Claim 21 is amended herein to indicate gpIIb/IIIa is glycoprotein IIb/IIIa, rendering the above rejection moot. Therefore, the basis of the rejection may be removed.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 21-33 are rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement for reasons of record. Specifically, the Examiner argues that the prior art of record fails to show a method of preventing gpIIb/IIIa-associated disorders in a mammal, by administering to a mammal an effective amount of adenosine; there is no predictability that using adenosine will work in specifically and differentially preventing gpIIb/IIIa-associated disorders in mammals. The Examiner asserts that there is insufficient guidance in the specification and that no working examples in mammals provided. Finally, the Examiner asserts that the specification fails to disclose the mode or mechanism or dosage at which adenosine can differentially and effectively prevent, as opposed to effectively treat gpIIb/IIIa-associated disorders. Applicants traverse this rejection.

Applicants respectfully submit that the present invention of inhibiting gpIIb/IIIa is reasonably enabled by the disclosure in the specification because adequate guidance is provided as well as working examples in mammals. First, the specification provide adequate guidance as to the making and using of the claimed invention. The specification details the extraction of adenosine from *Carthamus tinctorius L* at page 6, line 29 to line 37. The route, dosage, and formulation of adenosine in the claimed invention is disclosed at page 7, line 36 to page 8, line 10. Second, working examples of the extraction and *in vitro* analysis are provided in Examples 1-6 and Example 8 using routine methods recognized by one of ordinary skill in the art. Example 8 demonstrates specific inhibition of gpIIb/IIIa inhibition through the analysis of gpIIb/IIIa binding to fibrinogen. It is well known that fibrinogen binding is required for activation of gpIIb/IIIa, and therefore an assay such as this would be credible to the skilled artisan regarding the ability of adenosine to inhibit gpIIb/IIIa activation. Most importantly, the specification discloses a working example of adenosine as an anti-thrombotic in a model of

venous thrombosis induced by an electrical pulse in a mammal, *i.e.*, a rat. Any experimentation required to practice the claimed methods is routine. In view of the disclosure and the working examples, the disclosure reasonably enables the claimed invention.

In view of the above, Applicants request the withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102

Claims 21-30 are rejected under 35 U.S.C. § 102 (b) as allegedly being inherently anticipated by Sollevi, U.S. Patent No. 5,731,296. According to the Examiner, Sollevi discloses administering to human beings an effective amount of adenosine by continuous infusion for use in various disease conditions, including the inhibition of platelet aggregation (anti-aggregatory effect), antithrombotic effect (inhibit clot formation), vasodilation, peripheral and cardiovascular effects, and hypotensive activity. The Examiner also asserts that Sollevi discloses administering adenosine to a patient as a pharmaceutical composition and in combination with another antithrombotic. The Examiner acknowledges that Sollevi is silent in teaching that adenosine is effective in inhibiting the activation of platelet membrane receptor protein gpIIb/IIIa. Claims 21-25 are also rejected under 35 U.S.C. § 102 (b) as allegedly inherently anticipated by Wang et al. According to the Action, Wang teaches the administration of adenosine has an anti-thrombotic effect in dogs as an *in vivo* model of arterial thrombosis. Again, the Examiner acknowledges that Sollevi is silent in teaching that adenosine is effective in inhibiting the activation of platelet membrane receptor protein gpIIb/IIIa. Applicants traverse this rejection.

Applicants respectfully submits that Sollevi fails to teach or suggest each and every element of the claimed invention. More specifically, Sollevi fails to teach or suggest the use of adenosine to inhibit the activation of gpIIb/IIIa. Sollevi teaches the use of adenosine as a potent vasodilatory agent. *See* col. 20, lines 15-27. Sollevi states the vasodilatory effect of Sollevi

permits "good blood flow through the treated vessel, which in turn prevents platelet deposition on the traumatized vessel site." *See* col. 15-18. Alternatively stated, Sollevi teaches that adenosine acts an anti-thrombotic through vasodilation alone. While Sollevi suggests that adenosine has an inhibiting effect on platelet aggregation, there is no indication that this is a separate function from its vasodilatory effect. Thus, there is no teaching or suggestion that adenosine acts to inhibit platelet aggregation in any other circumstance other than vasoconstriction. It is well known in the art that platelet aggregation can be triggered by numerous distinct events. Such events include not only vasoconstriction, but also infection, septic shock, classical and occult myeloproliferative disorders, antiphospholipid syndrome, protein C, protein S and antithrombin deficiencies, and factor V Leiden, factor II, and methylene-tetrahydrofolate-reductase gene mutations. Sollevi contains no teaching or suggestion regarding these non-vasoconstriction mediated conditions that trigger thromboembolic events. Therefore, Sollevi does not anticipate the claimed invention.

Similarly, Wang fails to teach or suggest each and every element of the claimed invention. As acknowledged by the Examiner, Wang also fails to teach that adenosine is effective in inhibiting gpIIb/IIIa activation. Wang examines an animal model of stenosis or vasoconstriction.[1] As discussed above, the teaching of use of adenosine in vasoconstriction does not teach or suggest that adenosine inhibits gpIIb/IIIa. In the absence of such teaching, Wang does not anticipate the claimed invention.

In view of the above, Applicants request the withdrawal of this rejection.

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[1] The term "stenosis" is defined as an abnormal narrowing of a duct or canal. *See* DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 1757 (30th Ed. 2003). Thus, this is a constriction of the vessel or vasoconstriction.

Rejection Under 35 U.S.C. § 103

Claims 31-33 are rejected under 35 U.S.C. § 103 as allegedly being unpatentable over Sollevi, U.S. Patent No. 5,731,296, in view of Foster, 4,444,879. According to the Examiner, Foster discloses the incorporation of the adenosine composition and pharmaceutically acceptable carrier into a kit format. The Examiner asserts that it would be obvious to one of ordinary skill in the art to incorporate adenosine, antithrombotics, pharmaceutical carriers, and containers taught by Sollevi into a kit arrangement taught by Foster. Applicants traverse this rejection.

For the reasons discussed above, Sollevi does not teach or suggest the use of adenosine as an inhibitor of gpIIb/IIIa activation, and therefore the combination of Sollevi and Foster do not teach or suggest each and every element of the claimed methods. Hence, the cited combination fails to establish *prima facie* obviousness. As these claims are cancelled herein, this rejection is rendered moot.

In view of the above, Applicants request the withdrawal of this rejection.

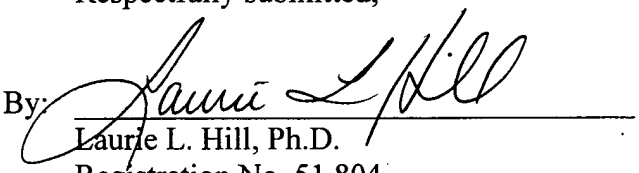
CONCLUSION

In view of the above, each of the claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejections of the claims and to pass this application to issue.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 205032000420.

Respectfully submitted,

Dated: December 10, 2003

By: 

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